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Neuroendocrine Tumour of the Appendix: A Case Report and Review of Literature

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Authors' contributions

This work was carried out in collaboration between all authors. Author RAV conceptualized and wrote the first draft of the manuscript. The other authors, JAN, BAO, BU and BAE participated in the review, editing and preparation of the final manuscript. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Neuroendocrine tumour of the appendix is a rare neoplasm discovered only incidentally. We hereby report an occurrence of this tumour in the appendix of a 27 years old female. There was an initial diagnosis of acute appendicitis based on a few days history of right abdominal quadrant pain, anorexia, vomiting and low-grade fever. The vermiform appendix obtained after an emergency appendectomy was large and had a firm yellowish mass, 1.6 cm in diameter. Histology revealed an appendiceal neuroendocrine tumour that had involved the mucosa, submucosa and part of the muscularis propria.

Keywords: Neuroendocrine tumour; carcinoid tumour; appendix; acute appendicitis.

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1. INTRODUCTION

Neuroendocrine neoplasms consist of a rare heterogeneous group of tumours, which arise from enterochromaffin or enterochromaffin-like cells, found in tissues of endodermal origin. The sites of occurrence of this disease include the bronchial tree in the lungs and gastrointestinal tract, including the appendix. Appendiceal neuroendocrine tumours (NETs) are classified into the classical NETS, tubular and goblet cell carcinoids [1]. The World Health Organisation 2010 classification divides neuroendocrine tumours of the appendix into well-differentiated neuroendocrine neoplasms (grades 1, 2 and 3), poorly differentiated neuroendocrine neoplasms and mixed andenoneuroendocrine carcinoma (MANEC). The criteria for the grading of the well-differentiated tumours are based on mitotic counts or Ki-67 labelling index [2]. The case report below is that of a neuroendocrine neoplasm of the appendix in a young female adult, initially thought to be acute appendicitis but later found to be this rare disease on histological examination of the specimen.

2. CASE REPORT

A twenty-seven years old female presented at the Accident and Emergency department of the Bingham University Teaching Hospital, Jos, Nigeria, with complaints of right abdominal pain. There was a few days history of anorexia, vomiting and low-grade fever. Physical examination revealed rebound tenderness in the right lower quadrant of the abdomen prompting the diagnosis of acute appendicitis. The appendix was removed through an open appendectomy.

2.1 Gross Pathology Features

The vermiform appendix, with the mesoappendix attached, was fixed in 10% formalin. The appendix was firm, enlarged, and had hyperaemic blood vessels on the surface. It measured 5cm in length and 1.8 cm largest diameter. The cut surface showed an obliterated lumen, with the substance of the appendix almost replaced by a circumscribed yellowish tumour (Fig. 1). The tumour measured 1.6 cm in diameter and involved most of the length of the appendix. The tumour was classified as stage T1b, following the European Neuroendocrine Tumour Society (ENETS) classification scheme [3].

2.2 Histopathology

The tissue was processed and stained with routine hematoxylin and eosin stains. Microscopy showed a circumscribed sheet of small uniform round cells arranged in small nests separated by thin connective tissue stroma (Fig. 2). There was characteristic retraction of these tumour cell clusters from the stroma. The cells had scant cytoplasm and small monotonous nuclei with acidophilic granules (Fig. 3). Although the muscle wall was involved, there was no spread to the surface of the organ. An average of three mitotic counts per high power field was obtained. The resection margin was free from neoplastic cells. The tumour was reported as a well-differentiated neuroendocrine tumour grade 2 (intermediate) based on the World Health Organisation (WHO) 2010 classification scheme for neuroendocrine neoplasms (NEN) [2].

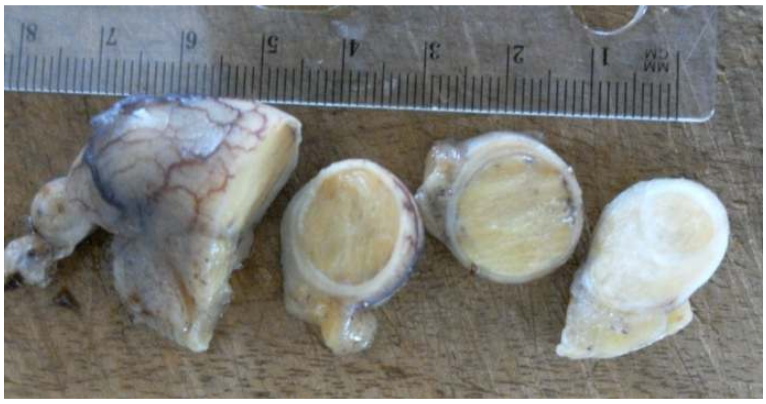

Fig. 1. Appendiceal Carcinoids: Gross image of appendix cut section showing the formalin fixed appendix filled with the yellow coloured well-defined tumour mass

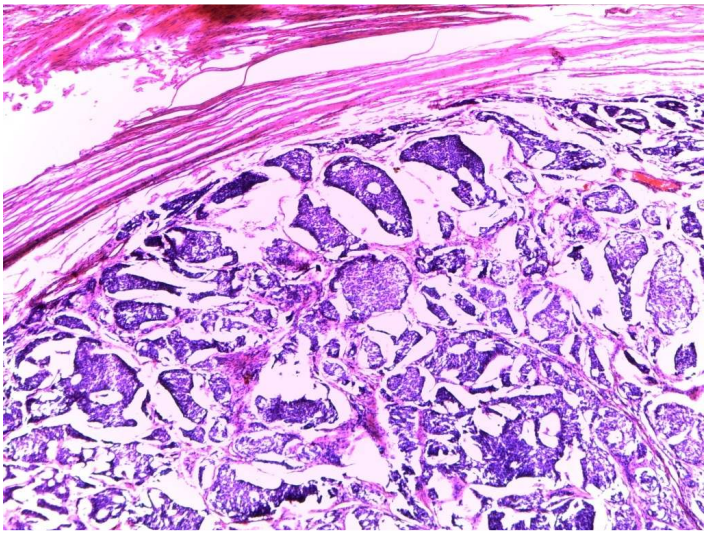

Fig. 2. Neuroendocrine tumour of the Appendix: This shows the irregular nests of small uniform cells exhibiting retraction from the surrounding stroma. [*Hematoxylin and eosin stain, x 4 objective magnification*]

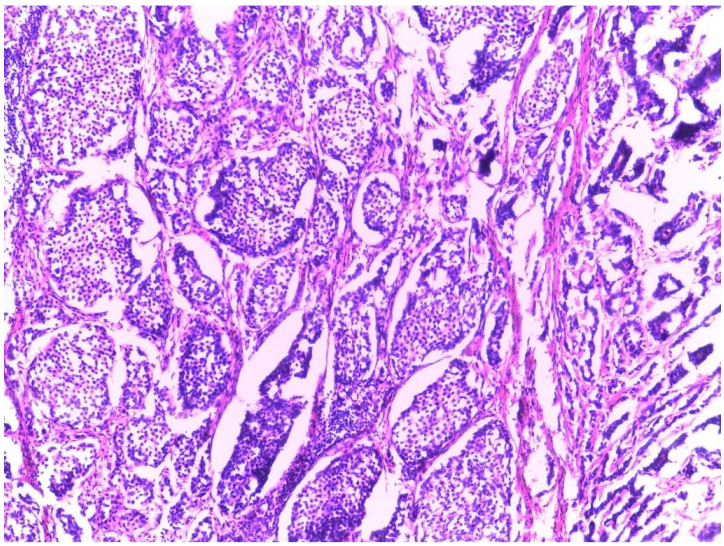

Fig. 3. Neuroendocrine tumour of the Appendix: The monotonous cells within these clusters are characterised by scant cytoplasm, minimal nuclear pleomorphism and coarse chromatin distribution. [*Hematoxylin and eosin stain, x 10 objective magnification*]

Since symptoms of carcinoid syndrome were absent, a simple appendectomy was regarded as a sufficient treatment. The patient was lost to follow-up.

3. DISCUSSION AND REVIEW OF LITERATURE

Acute appendicitis constitutes a significant proportion of solid surgical specimens received in the pathology laboratory [4]. There is a wide age variation in the occurrence of appendicitis but many studies have pointed to a higher frequency among young adults. Mean ages of 25 (±12.3) years, 25.79 years, and 26.33 (±11.39) years have been reported previously from different centres in Nigeria [4,5,6]. The diagnoses commonly stated on histopathology reports include normal appendix, acute appendicitis, acute suppurative appendicitis, and appendix

with lymphoid hyperplasia [7]. However, obstruction of the lumen by impacted faecalith has been shown in many reports to be the cause in most surgically removed appendices [2]. Infections, parasitic infestations and tumours, may present with the classical features of acute appendicitis [6,8,9]. In addition, a carcinoid tumour may co-exist with this condition [10].

A Swiss pathologist, Theodor Langhans first described this tumour in 1867 and Obendorfer called it “carcinoid” tumour in 1907 [11]. The term “neuroendocrine neoplasm” (NEN) has now been widely accepted as the appropriate nomenclature for this category of neoplasms because these tumours all have a malignant potential, although some may be benign [2].

Marshall et al. [12] reviewed 55 cases of gastrointestinal carcinoids with complete follow-up and observed that 19 (35%) cases occurred in the ileum, while 17 cases (31%) occurred in the appendix.

The National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) programme database shows appendiceal neuroendocrine neoplasms to have an incidence rate of approximately 0.15/100,000/year [13]. The condition is more common within the age range of 40 to 50 years. They are more common in females [3].

The tumour in the reported case was about 1.6 cm in diameter, and had obliterated the lumen of the appendix completely [2]. In the TNM staging of the WHO 2010 classification of neuroendocrine neoplasms (NEN), a primary tumour of more than 1 cm but not more than 2cm is categorised as T1b [2]. Some authors, in a review article on endocrine tumours of the appendix, observed that the size distribution of carcinoids was 60% - 80% for tumours less than 1cm, 4% - 37% for those between 1cm and 2 cm, and 2% - 17% for those larger than 2cm [14]. A series of original research and review papers by several authors have established the prognostic importance of the size of the tumour [15,16,17]. The other factors, which may affect prognosis, include the involvement of the serosa, mesoappendix or extension to adjacent organs or peritoneum [13]. Metastasis to distant sites such as the liver, though quite rare, has also been reported [18]. In addition, the frequency of metastasis has been related to tumour sizes greater than 2 cm and invasion of the mesoappendix [3,18]. While most authors consider tumour size to be the major prognostic factor, Volante et al concluded that the size of the tumour is actually less important in predicting the clinical outcome based on their retrospective multi-institutional analysis of 138 appendiceal neuroendocrine neoplasms. This group surmised that adverse outcome was significantly associated with extramural extension (including the mesoappendix), well differentiated carcinoma diagnosis, positive resection margins, but not with tumour size, mitotic or proliferative indexes [19].

The tumour in the case reported did not extend beyond the muscularis propria and there were no clinical features suggestive of a carcinoid syndrome. Overall, the case had the indicators of an appendiceal endocrine neoplasm with a good prognosis. The surgeon considered a simple appendectomy as a sufficient treatment. European Neuroendocrine Tumour Society (ENETS) consensus guidelines recommends simple appendectomy for T1 (ENETS) or T1a (UICC/AJCC) [3]. The finding of a neuroendocrine tumour in the appendix represents an instance of a classical medical serendipity, as most reported cases were discovered incidentally during microscopy [12]. Tumours more advanced than stage T2 neoplasms may require right hemicolectomy because of the increased risk of distant metastasis, lymph node metastasis and long-term tumour recurrence. Meanwhile, for stage T2 (ENETS) or T1b (UICC/AJCC) tumours, the decision on whether a right hemicolectomy will be performed or not depends on the tumour stage and size, status of the resection margins, involvement of the mesoappendix, lymph node matastasis and perioperative risks [3]. Histological observation of lymphatic and blood vessel invasion has been noted to be independent risk factors for lymph node metastasis in colorectal and appendiceal NETs in a study of 760 neuroendocrine tumours [20]. A recent review also showed conflicting evidence on the best management for tumours greater than 2 cm; however, ENETS advocates right hemicolectomy for all tumours greater than this size [21].

4. CONCLUSION

We have presented a rare case of an incidentally discovered neuroendocrine tumour of the appendix in a 27 years old female mimicking acute appendicitis.

CONSENT

As per international standard or university standard written patient consent has been collected and preserved by the authors.

ETHICAL APPROVAL

Ethical clearance was obtained from the institution's research ethics committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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